CLAIMS:

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. A method for rendering a subpopulation of primary mammalian cells susceptible to drug-induced growth, proliferation or differentiation,

which method comprises transducing one or more cells of a population of primary mammalian cells with at least one recombinant DNA construct encoding a fusion protein which comprises at least one signaling domain and at least one drug-binding domain which is heterologous with respect to the signaling domain and binds to a selected drug, wherein exposure of the transduced cells to the drug induces growth, proliferation or differentiation of said cells.

2. The method of Claim 1 wherein the drug is characterized by one or more of the following:

(a) the drug is not a protein,

(b) the drug has a molecular weight less than 5 kD, and,

(c) the drug is cell-permeant.

3. The method of Claim 1 wherein the population of primary mammalian cells comprises hemopoietic cells, hepatic cells, muscle cells, nerve cells, cartilage and/or bone cells, intestinal cells, pancreatic cells or kidney cells, or a subpopulation of cells obtained therefrom.

4. The method of Claim 3 wherein the population of primary mammalian cells comprises bone marrow cells, cord blood cells, peripheral blood cells or a subpopulation of cells obtained from either.

5. The method of Claim 1 wherein the primary mammalian cells are human cells.

6. The method of Claim 1 wherein the drug is multivalent and binds to two or more fusion protein molecules, each of which fusion protein molecules comprises at least one drug-binding domain.

7. The method of Claims 1 wherein the drug has substantially no pharmacologic activity on non-engineered mammalian cells.

8. The method of Claim 1 wherein the signaling domain comprises any domain capable of stimulating growth, proliferation or differentiation upon multimerization.

9. The method of Claim 8 wherein the signaling domain comprises at least the cytoplasmic portion of a receptor for a growth or differentiation factor.

10. The method of Claim 9 wherein the receptor is a receptor for a colony stimulating factor.

11. The method of Claim 9 wherein the receptor protein is c-kit, gp130 or flt-3, or a receptor for EGF, FGF, CSF-1, G-CSF, thrombopoietin, erythropoietin, growth hormone, prolactin or hepatocyte growth factor.

12. The method of Claim 1 wherein the cells are removed from the mammal prior to being transduced with the recombinant DNA construct(s).

13. The method of Claim 12 which further comprises introducing the transduced cells so obtained into a mammal.

14. The method of Claim 13 wherein the transduced cells are treated with drug prior to their introduction into the mammal.

15. The method of Claim 13 wherein the cells are allogeneic with respect to the mammal.

16. The method of Claim 13 wherein the cells are syngeneic with respect to the mammal.

17. The method of Claim 13 wherein the cells are autologous with respect to the mammal.

18. The method of Claim 13 wherein the mammal is a human.

19. The method of Claim 1 wherein the cells are transduced within the mammal.

20. The method of Claim 19 wherein the cells are transduced by administration of the recombinant DNA construct to the mammal using one or more viral vectors.

21. A method for expanding a subpopulation of primary mammalian cells comprising:

(a) providing a subpopulation of primary mammalian cells which contain at least one recombinant DNA construct encoding a fusion protein which (a) comprises at least one signaling domain and at least one drug-binding domain, and (b) induces growth, proliferation or differentiation upon multimerization with one or more other fusion proteins containing at least one signaling domain; and

(b) treating the subpopulation of cells with the drug.

22. A method for expanding a subpopulation of primary mammalian cells comprising:

(a) providing a subpopulation of primary mammalian cells which contain at least one recombinant DNA construct encoding a fusion protein comprising at least one signaling domain and at least one drug-binding domain which binds to a selected drug,

wherein the drug is characterized by one or more of the following:

(i) the drug is not a protein,

(ii) the drug has a molecular weight less than 5 kD, and,

(iii) the drug is cell-permeant; and

wherein exposure of the transduced cells to the drug induces growth, proliferation or differentiation of said cells; and,

(b) exposing the transduced cells to the drug.

23. The method of Claim 21 wherein the population of primary mammalian cells comprises hemopoietic cells, hepatic cells, muscle cells, nerve cells, cartilage and/or bone cells, intestinal cells, pancreatic cells or kidney cells, embryonic stem cells, or a subpopulation of cells obtained therefrom.

24. The method of Claim 23 wherein the population of primary mammalian cells comprises bone marrow cells, cord blood cells, peripheral blood cells, or a subpopulation of cells obtained from either.

25. The method of Claim 21 wherein the primary mammalian cells are human cells.

26. The method of Claim 21 wherein the drug is multivalent and binds to two or more fusion protein molecules, each of which fusion protein molecules comprises at least one drug-binding domain.

27. The method of Claim 21, wherein the drug has substantially no pharmacologic activity, other than the activity of inducing signaling triggered by multimerization of the fusion proteins.

28. The method of Claim 21 wherein the signaling domain comprises any domain capable of stimulating growth, proliferation or differentiation upon multimerization.

29. The method of Claim 28 wherein the signaling domain comprises at least the cytoplasmic portion of a receptor for a growth or differentiation factor.

30. The method of Claim 29 wherein the receptor is a receptor for a colony stimulating factor.

31. The method of Claim 29 wherein the receptor protein is c-kit, gp130 or flt-3, or a receptor for EGF, FGF, CSF-1, G-CSF, thrombopoietin, erythropoietin, growth hormone, prolactin or hepatocyte growth factor.

32. The method of Claim 21 wherein the cells are removed from the mammal prior to the transduction thereof with the recombinant DNA construct(s).

33. The method of Claim 32 which further comprises introducing the transduced cells so obtained into a recipient mammal.

34. The method of Claim 33 wherein the transduced cells are treated with the drug prior to their introduction into the recipient mammal.

35. The method of Claim 33 wherein the cells are allogeneic with respect to the mammal.

36. The method of Claim 33 wherein the cells are syngeneic with respect to the mammal.

37. The method of Claim 33 wherein the cells are autologous with respect to the mammal.

38. The method of Claim 33 wherein the mammal is a human.

39. The method of Claim 21 wherein the cells are transduced within the mammal.

40. The method of Claim 39 wherein the cells are transduced by administration of the recombinant DNA construct(s) to the mammal using one or more viral vectors.

41. The method of Claim 21, wherein the cells are treated with the drug *ex vivo*.

42. The method of Claim 21, wherein the cells are treated with the drug *in vivo*.

43. The method of Claim 21, wherein the cells contain an additional heterologous DNA or RNA construct.

44. A genetically engineered primary mammalian cell containing a recombinant DNA construct encoding a fusion protein consisting of at least one drug binding domain for binding to a selected drug and at least one signaling domain, wherein administration of the drug to the cell induces its growth, proliferation and/or differentiation.

45. The cell of Claim 44 wherein the primary mammalian cell is selected from the group consisting of hemopoietic cells, hepatic cells, muscle cells, nerve cells, cartilage and/or bone cells, intestinal cells, pancreatic cells and kidney cells, embryonic stem cells, or a subpopulation of cells obtained therefrom.

46. The cell of Claim 45 wherein the primary mammalian cell is a bone marrow cell, a cord blood cell or a peripheral blood cell.

47. The cell of Claim 44 wherein the primary mammalian cell is a human cell.

48. The cell of Claim 44 wherein the drug is multivalent and binds to two or more fusion protein molecules, each of which fusion protein molecules comprises at least one drug-binding domain.

49. The cell of Claim 44 wherein the drug has substantially no pharmacologic activity other than the activity of inducing signaling triggered by multimerization of the fusion proteins.

50. The cell of Claim 44 wherein the signaling domain comprises any domain capable of stimulating growth, proliferation or differentiation upon multimerization.

51. The cell of Claim 50 wherein the signaling domain comprises at least the cytoplasmic portion of a receptor for a growth or differentiation factor.

52. The cell of Claim 51 wherein the receptor is a receptor for a colony stimulating factor.

53. The cell of Claim 52 wherein the receptor protein is c-kit, gp130 or flt-3, or a receptor for EGF, FGF, CSF-1, G-CSF, thrombopoietin, erythropoietin, growth hormone, prolactin or hepatocyte growth factor.

54. The cell of Claim 44 which contains an additional heterologous DNA or RNA construct.

55. An *ex vivo* culture of genetically engineered primary cells of any of Claims 44-54.

56. A method for treating or preventing a hemopoietic disease or pathological condition in a mammal, comprising introducing into the mammal the bone marrow cell or cord blood cell or peripheral blood cell of Claim 46.

57. A method of Claim 56 which further comprises administering to the mammal a dimerizing drug which binds to the fusion protein and thereby induces the growth, prolifieration or differentiation of the cell.

58. The method of Claim 56 wherein the hemopoietic disease is selected from the group consisting of thrombocytopenia, leukopenia, leukemia, beta

thalassemia, sickle cell anemia, Fanconi anemia, aplastic anemia, myelodysplastic syndrome, chronic granulomatous disease, leukocyte adhesion deficiency.

59. A method for treating or preventing a hemopoietic disease or pathological condition in a mammal, comprising expanding a subpopulation of hemopoietic cells by the method of Claim 24 and introducing the resultant cells to the mammal.

60. A method for obtaining a population of megakaryocytes, comprising expanding a subpopulation of bone marrow cells by the method of Claim 24 for a sufficient period of time permitting the growth of a population of cells enriched for megakaryocytes.

61. A method for obtaining a population of neutrophils, comprising expanding a subpopulation of bone marrow cells by the method of Claim 24 for a sufficient period of time permitting the growth of a population of cells enriched for neutrophils.

62. A method for obtaining a population of erythroid cells, comprising expanding a subpopulation of cord blood cells by the method of Claim 24 for a sufficient period of time permitting the growth of a population of cells enriched for erythroid cells.

63. A method for treating a hemopoietic disease or pathological condition in a mammal comprising:

(a) providing a subpopulation of mammalian bone marrow or cord blood cells or peripheral blood cells that contain at least one recombinant DNA construct encoding a fusion protein that (i) comprises at least one signaling domain and at least one domain, heterologous thereto, for binding to a selected drug, and (ii) induces growth, proliferation or differentiation upon multimerization with one or more other fusion proteins containing at least one signaling domain;

(b) introducing said cells into a mammal in need thereof; and

(c) administering to said mammal with the selected drug.

64. A method of Claim 63 which is repeated one or more times.

65. A method for rendering a mammal susceptible to treatment for hemopoietic disease, comprising providing said mammal with bone marrow or cord blood or peripheral blood cells genetically engineered to contain a construct encoding a fusion protein consisting of at least one drug binding domain for binding to a selected drug and at least one signaling domain wherein binding of the drug to the drug binding domain induces oligomerization of the signaling domain and proliferation of the cells.

66. A method for treating a hemopoietic disease, comprising administering to a patient that has been made susceptible for treatment for a hemopoietic disease by the method of Claim 63 a drug that binds said drug binding domain.

67. The method of Claim 66, wherein the engineered cells also contain an additional heterologous DNA or RNA construct.

68. The method of Claim 67, wherein the heterologous DNA construct encodes a gene capable of correcting a genetic defect.

69. The method of Claim 68, wherein the DNA construct encodes the gene for globin.

70. An improved method for administering hemopoietic stem cell therapy to a mammal which comprises:

(a) harvesting a composition from a donor mammal which comprises hemopoietic stem and/or progenitor cells;

(b) transducing the harvested cells with at least one recombinant DNA construct encoding a fusion protein which (i) comprises at least one signaling domain and at least one domain, heterologous thereto, for binding to a selected drug, and (ii) induces growth, proliferation or differentiation upon multimerization with one or more other fusion proteins containing at least one signaling domain;

(c) introducing the transduced cells into a recipient mammal; and

(d) administering the selected drug to the recipient mammal.

71. The method of Claim 70, wherein the mammal is human.

72. The method of Claim 70, wherein the donor mammal and recipient mammal are the same.

73. The method of Claim 70, wherein the donor mammal is subjected to stem cell mobilization prior to harvesting.

74. The method of Claim 70, wherein the harvested composition is enriched for stem and/or progenitor cells prior to transducing with recombinant DNA(s).

75. The method of Claim 70, wherein the transduced cells are subjected to one or more treatments with a dimerizing drug prior to introduction of the cells into the recipient mammal.

76. The method of Claim 70, wherein the method is repeated one or more times.

77. An improved method for treating a neurodegenerative disease or disorder in a mammal which comprises:

(a) harvesting a composition from a donor mammal or from mammalian embryonic tissue which comprises stem and/or progenitor cells of the CNS;

(b) transducing the harvested cells with at least one recombinant DNA construct encoding a fusion protein which (i) comprises at least one signaling domain and at least one domain, heterologous thereto, for binding to a selected drug, and (ii) induces growth, proliferation or differentiation upon multimerization with one or more other fusion proteins containing at least one signaling domain;

(c) introducing the transduced cells into a recipient mammal; and

(d) administering the selected drug to the recipient mammal.

78. The method of Claim 77, wherein the composition is harvested from mammalian embryonic tissue.

79. The method of Claim 77, wherein the harvested composition is enriched for stem and/or progenitor cells of interest prior to transducing with recombinant DNA(s).

80. The method of Claim 77, wherein at least one fusion protein comprises a signaling domain derived from a receptor for neurotrophin-3, bFGF, thyroid hormone T3 or ciliary neurotrophic factor.

81. The method of Claim 77, wherein the donor and recipient are human.

82. The method of Claims 77, wherein the transduced cells are subjected to one or more treatments with a dimerizing drug prior to introduction of the cells into the recipient mammal.

83. A method for rendering a subpopulation of human embryonic stem cells susceptible to drug-induced growth, proliferation or differentiation, comprising transducing one or more cells of the subpopulation with at least one recombinant DNA construct encoding a fusion protein which comprises at least one signaling domain and at least one drug-binding domain which is heterologous with respect to the signaling domain and binds to a selected drug, wherein exposure of the transduced cells to the drug induces growth, proliferation or differentiation of said cells.

84. The method of Claim 83 wherein the drug is characterized by one or more of the following:

(a) the drug is not a protein,

(b) the drug has a molecular weight less than 5 kD, and,

(c) the drug is cell-permeant.

85. The method of Claims 82, wherein the transducer cells are subjected to one or more treatments with a dimerizing drug prior to introduction of the cells into the recipient mammal.

86. The method of Claims 82, wherein the fusion protein comprises a signaling domain capable of stimulating differentiation of the transduced human embryonic stem cells into endoderm, mesoderm or ectoderm cells.

87. An improved method for treating human disease or disorder which comprises:

(a) harvesting embryonic stem cells,

(b) transducing the harvested cells with at least one recombinant DNA construct encoding a fusion protein which (i) comprises at least one signaling domain and at least one domain, heterologous thereto, for binding to a selected drug, and (ii) induces differentiation and growth of the harvested cells into endoderm, mesoderm or ectoderm cells upon multimerization with one or more other fusion proteins containing at least one signaling domain;

(c) introducing the transduced cells into a recipient human; and

(d) administering the selected drug to the recipient human.

88. The method of Claims 87, wherein the transduced cells are subjected to one or more treatments with a dimerizing drug prior to introduction of the cells into the recipient mammal.